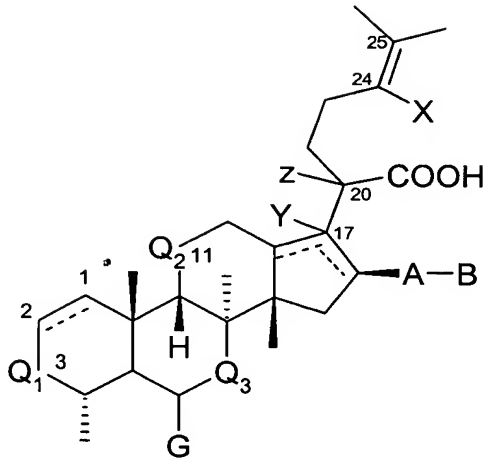
CLAIMS

1. A compound of general formula I



[I]

wherein X represents halogen, trifluoromethyl, cyano, azido, alkyl, alkenyl or aryl, wherein said alkyl, alkenyl or aryl are optionally substituted by one or more, same or different substituents selected from the group consisting of alkyl, alkenyl, aryl, alkoxy, nitro, alkylthio, halogen, azido, trifluoromethyl and cyano;

Y and Z both represent hydrogen, or together with the C-17/C-20 bond form a double bond between C-17 and C-20, or together are methylene and form a cyclopropane ring in combination with C-17 and C-20;

A represents a bond, O, S or S(O);

B represents C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} acyl, C_{3-7} cycloalkylcarbonyl or benzoyl, all of which are optionally substituted with one or more substituents selected from the group consisting of halogen, hydroxy, alkoxy, aryl, heteroaryl and azido, or, if A represents a bond, B may also represent hydrogen;

Q_1 and Q_2 independently represent $-CH_2-$, -C(O)-, -(CHOH)-, -(CHOR)-, -(CHSH)-, -(NH)-,

$-(CHNH_2)-$ or $-(CHW)-$, wherein R represents C_{1-6} alkyl and W represents halogen, cyano, azido or trifluoromethyl;

Q_3 represents $-CH_2-$, -C(O)- or -CHOH-;

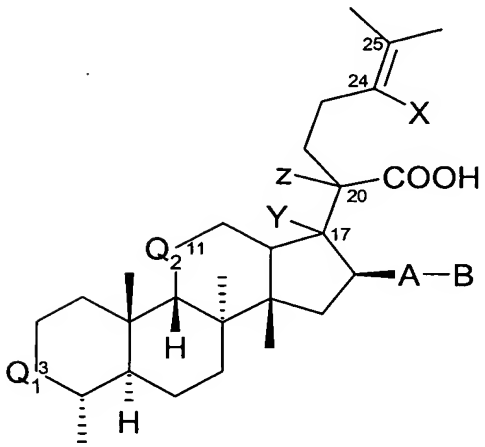
G represents hydrogen, OH or $O-CO-CH_3$;

two bonds in the pentacyclic ring being depicted with full and dotted lines to indicate that either of the two bonds may be a double bond, in which case Y is absent and Z represents hydrogen;

the bond between C-1 and C-2 being either a single or a double bond;

and pharmaceutically acceptable salts and easily hydrolysable esters thereof.

2. A compound according to claim 1 of formula Ia



[Ia]

wherein X represents halogen, trifluoromethyl, cyano, azido, C_{1-7} alkyl, C_{2-9} alkenyl or aryl, wherein said C_{1-6} alkyl, C_{2-6} alkenyl or aryl are optionally substituted by one or more, same or different substituents selected from the group consisting of C_{1-7} alkyl, C_{2-9} alkenyl, aryl, C_{1-6} alkoxy, nitro, alkylthio, halogen, azido, trifluoromethyl and cyano;

Y and Z both represent hydrogen, or together with the C-17/C-20 bond form a double bond between C-17 and C-20, or together are methylene and form a cyclopropane ring in combination with C-17 and C-20;

A represents a bond, O, S or S(O);

B represents C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} acyl, C_{3-7} cycloalkylcarbonyl or benzoyl, all of which are optionally substituted with one or more substituents selected from the group consisting of halogen, hydroxy, C_{1-6} alkoxy, aryl, heteroaryl and azido, or, if A represents a bond, B may also represent hydrogen;

Q_1 and Q_2 independently represent -C(O)-, -(CHOH)-, -(CHSH)-, or –(CHW)-, wherein W represents halogen, cyano, azido or trifluoromethyl;

and pharmaceutically acceptable salts and easily hydrolysable esters thereof.

3. A compound according to claim 1 or 2, wherein Y and Z are both hydrogen and wherein the stereochemical configuration is S at both C-17 and C-20.

4. A compound according to claim 1 or 2, wherein Y and Z together are methylene and form a cyclopropane ring in combination with C-17 and C-20 and the stereochemical configuration is S at both C-17 and C-20.

5. A compound according to claim 1 or 2, wherein Y and Z together with the C-17/C-20 bond form a double bond between C-17 and C-20.

6. A compound according to claim 5, wherein the C-17/C-20 double bond has the same configuration as in fusidic acid.

7. A compound according to claim 1 or 2, wherein X represents chloro, bromo, iodo, fluoro, methyl, ethyl, propyl, phenyl, vinyl, propenyl, butenyl, pentenyl, hexenyl, heptenyl, nonenyl, biphenyl or naphthyl, wherein said methyl, ethyl, propyl, phenyl, vinyl, propenyl, butenyl, pentenyl, hexenyl, heptenyl, nonenyl, biphenyl or naphthyl, are optionally substituted by one or more, same or different substituents selected from the group consisting of fluoro, chloro, bromo, phenyl, vinyl, cyano, methoxy, trifluoromethyl, nitro, methylthio, butyl, methyl, ethyl, propyl, butyl, pentyl, hexyl, and heptyl.

8. A compound according to claim 7, wherein X represents fluoro, chloro, bromo, iodo, trifluoromethyl, phenyl, 4-bromophenyl, 4-chlorophenyl, 3,5-difluorophenyl, *trans*-1-hexen-1-yl, *trans*-1-buten-3,3-dimethyl-1-yl, *trans*-1-nonen-1-yl, *trans*-5-chloro-1-penten-1-yl, *trans-2*-phenyl-1-vinyl, 2-phenyl-1-ethyl, 4-*n*-propylphenyl, 4-vinylphenyl, 4-*tert*-butylphenyl, 4-cyanophenyl, 3-biphenyl, 4-(trifluoromethyl)phenyl, 4-methoxyphenyl, 3-cyanophenyl, 2-methoxyphenyl, 3-nitrophenyl, 3-bromophenyl, 4-(methylthio)phenyl, 2-naphtyl, 3,5-*bis*-(trifluoromethyl)phenyl, 3,4-dimethoxyphenyl or 3,5-dibromophenyl.

9. A compound according to claim 1 or 2, wherein Q_1 and Q_2 independently represent –C(O)- or –(CHOH)-.

10. A compound according to claim 1 or 2, wherein Q_1 represents CHF, CHCl, CHBr, CHI or CHN_3.

11. A compound according to claim 2, wherein Q_1 and Q_2 both represent a –(CHOH)- group, or one of Q_1 or Q_2 represents -(CO)-, or Q_1 represents CHF, CHCl, CHBr, CHI or CHN_3;

X represents chloro, bromo, iodo, trifluorometyl, azido or cyano;
Z and Y together with the C-17/C-20 bond form a double bond between C-17 and C-20;
A represents O, S or S(O);
B represents a C_{1-4} alkyl group, optionally substituted with one or more substituents selected from the list consisting of azido, hydroxy, fluoro, chloro and bromo, or B represents a C_{1-4} acyl group or a benzoyl group, both optionally substituted with one or more halogen atoms.

12. A compound according to claim 11, wherein the halogen atoms with which B is optionally substituted are fluoro or chloro.

13. A compound according to claim 1 or 2, wherein A represents O or S(O).

14. A compound according to claim 1 or 2, wherein B represents acyl, methyl, ethyl, propyl, butyl, pentyl, propenyl or cyclopentyl, all of which are optionally substituted with one or more substituents selected from the list consisting of methyl, ethyl, propyl, butyl, fluoro, vinyl, hydroxy, phenyl, furfuryl and methoxy.

15. A compound according to claim 14, wherein B is acetyl, isopropyl, ethyl, 2,2,2-trifluoroethyl, vinyl, 1-pentyl, 2-methyl-1-butyl, 3-methyl-1-butyl, cyclopentyl, 2-hydroxyethyl, benzyl, furfuryl, phenyl, 2-fluoroethyl, 2-methoxyethyl, 2,2,2-trichloroethyl, 2-azidoethyl, 2-hydroxyethyl, propyl, tert.-butyl, 1,3-difluoro-isopropyl, propionyl, chloroacetyl or trifluoroacetyl.

16. A compound according to claim 1 or 2, wherein Q_1 or Q_2 or both Q_1 and Q_2 represent –(COH)- and the stereochemical configuration is α at both C-3 and C-11.

17. A compound according to claim 1 or 2, wherein the easily hydrolysable ester is a pivaloyloxymethylester or a acetoxymethylester.

18. A compound according to claim 12, wherein A represents O, B is acetyl, wherein Q_1 or Q_2 or both Q_1 and Q_2 represent –(COH)- and the stereochemical configuration is α at both C-3 and C-11, Y and Z together with the C-17/C-20 bond form a double bond between C-17 and C-20 which has the same configuration as in fusidic acid.

19. A pharmaceutically acceptable salt of a compound according to claim 1 or 2, wherein the salts are selected from the group consisting of sodium salts, choline salts, L-arginine salts, 2-(dimethylamino)-ethanol salts, 4-(2-hydroxyethyl)-morpholin salts, L-lysine salts, N-(2-hydroxyethyl)-pyrrolidine salts, ethanolamine salts, potassium salts, tetrabutylammonium salts, benzyltrimethylammonium salts, cetyltrimethylammonium salts, tetramethylammonium salts, tetrapropylammonium salts, tris(hydroxymethyl)aminomethane salts, N-methyl-D-glucamine salts, silver salts, benzethonium salts and triethanolamine salts.

20. A compound according to claim 1, which is selected from the group consisting of

24-trifluoromethyl fusidic acid sodium salt (Compound 101),
24-trifluoromethyl fusidic acid pivaloyloxymethyl ester (Compound 102),
24-chloro-fusidic acid (Compound 103),
24-chloro-fusidic acid pivaloyloxymethyl ester (Compound 104),
24-chloro-fusidic acid sodium salt (Compound 105),
24-trifluoromethyl fusidic acid (Compound 106),
24-bromo-fusidic acid acetoxymethyl ester (Compound 107),
24-bromo-fusidic acid (Compound 108),
24-bromo-fusidic acid sodium salt (Compound 109),
24-bromo-fusidic acid pivaloyloxymethyl ester (Compound 110),
24-bromo-16-deacetoxy-16β-thioacetyl-fusidic acid acetoxymethylester (Compound 111),
24-bromo-16-deacetoxy-16β-isopropylthio-fusidic acid (Compound 112),
24-bromo-16-deacetoxy-16β-isopropylsulfinyl-fusidic acid (Compound 113),
24-bromo-16-deacetoxy-16β-thioacetyl-fusidic acid (Compound 114),
24-bromo-17S,20S-dihydrofusidic acid (Compound 115),
24-bromo-16-deacetoxy-16β-ethoxy-fusidic acid (Compound 116),
24-bromo-16-deacetoxy-16β-ethoxy-fusidic acid acetoxymethyl ester (Compound 117),
24-bromo-16-deacetoxy -16β-(2',2',2'-trifluoroethoxy)-fusidic acid acetoxymethyl ester (Compound 118),
24-bromo-16-deacetoxy -16β-(2',2',2'-trifluoroethoxy)-fusidic acid (Compound 119),
24-bromo-17S,20S-fusidic acid acetoxymethyl ester (Compound 120),

24-bromo-17S,20S-methylene-fusidic acid acetoxymethyl ester (Compound 121),
24-bromo-17S,20S-methylene-fusidic acid (Compound 122),
3-deoxy-3β,24-dibromo-fusidic acid (Compound 123),
3α-azido-24-bromo-3-deoxy-fusidic acid (Compound 124),
24-iodo-fusidic acid (Compound 125),
24-iodo-fusidic acid acetoxymethyl ester (Compound 126),
24-iodo-fusidic acid pivaloyloxymethyl ester (Compound 127),
24-phenyl-fusidic acid pivaloyloxymethylester (Compound 136),
24-phenyl-fusidic acid (Compound 137),
24-(4-bromophenyl)-fusidic acid pivaloyloxymethylester (Compound 138),
24-(4-bromophenyl)-fusidic acid (Compound 139),
24-(4-chlorophenyl)-fusidic acid pivaloyloxymethylester (Compound 140),
24-(4-chlorophenyl)-fusidic acid (Compound 141),
24-(3,5-difluorophenyl)-fusidic acid pivaloyloxymethylester (Compound 142),
24-(3,5-difluorophenyl)-fusidic acid (Compound 143),
3-deoxy-3β,24-dibromo-fusidic acid acetoxymethyl ester (Compound 144),
24-bromo-16-deacetoxy-16β-ethylthio-fusidic acid (Compound 146),
24-bromo-16-deacetoxy-16β-ethylsulfinyl-fusidic acid (Compound 147),
24-bromo-16-deacetoxy-16β-allylthio-fusidic acid (Compound 148),
24-bromo-16-deacetoxy-16β-(1-pentylthio)-fusidic acid (Compound 149),
24-bromo-16-deacetoxy-16β-(1-pentylsulfinyl)-fusidic acid (Compound 150),
24-bromo-16-deacetoxy-16β-(2-methyl-1-butylthio)-fusidic acid (Compound 151),
24-bromo-16-deacetoxy-16β-(2-methyl-1-butylsulfinyl)-fusidic acid (Compound 152),
24-bromo-16-deacetoxy-16β-(3-methyl-1-butylthio)-fusidic acid (Compound 153),
24-bromo-16-deacetoxy-16β-(3-methyl-1-butylsulfinyl)-fusidic acid (Compound 154),
24-bromo-16-deacetoxy-16β-cyclopentylthio-fusidic acid (Compound 155),
24-bromo-16-deacetoxy-16β-(2,2,2-trifluoroethylthio)-fusidic acid (Compound 156),
24-bromo-16-deacetoxy-16β-(2-hydroxyethylthio)-fusidic acid (Compound 157),
24-bromo-16-deacetoxy-16β-benzylthio-fusidic acid (Compound 158),
24-bromo-16-deacetoxy-16β-benzylsulfinyl-fusidic acid (Compound 159),
24-bromo-16-deacetoxy-16β-(2-furylmethylthio)-fusidic acid (Compound 160),
24-bromo-16-deacetoxy-16β-phenylthio-fusidic acid (Compound 161),
24-bromo-16-deacetoxy-16β-benzoylthio-fusidic acid (Compound 162),
24-bromo-16-deacetoxy-16β-isopropoxy-fusidic acid (Compound 163),
24-bromo-16-deacetoxy-16β-(2-fluoroethoxy)-fusidic acid (Compound 164),
24-bromo-16-deacetoxy-16β-(2-methoxyethoxy)-fusidic acid (Compound 165),
24-(*trans*-1-hexen-1-yl)-fusidic acid (Compound 166),

24-(*trans*-1-buten-3,3-dimethyl-1-yl)-fusidic acid (Compound 167),
24-(*trans*-1-nonen-1-yl)-fusidic acid (Compound 168),
24-(*trans*-5-chloro-1-penten-1-yl)-fusidic acid (Compound 169),
24-(*trans-2*-phenyl-1-vinyl)-fusidic acid (Compound 170),
24-(2-phenyl-1-ethyl)-fusidic acid (Compound 171),
24-(4-*n*-propylphenyl)-fusidic acid (Compound 172),
24-(4-vinylphenyl)-fusidic acid (Compound 173),
24-(4-*tert*-butylphenyl)-fusidic acid (Compound 174),
24-(4-cyanophenyl)-fusidic acid (Compound 175),
24-(3-biphenyl)-fusidic acid (Compound 176),
24-(4-(trifluoromethyl)phenyl)-fusidic acid (Compound 177),
24-(4-methoxyphenyl)-fusidic acid (Compound 178),
24-(3-cyanophenyl)-fusidic acid (Compound 179),
24-(2-methoxyphenyl)-fusidic acid (Compound 180),
24-(3-nitrophenyl)-fusidic acid (Compound 181),
24-(3-bromophenyl)-fusidic acid (Compound 182),
24-(4-(methylthio)phenyl)-fusidic acid (Compound 183),
24-(2-naphtyl)-fusidic acid (Compound 184),
24-(3,5-*bis*-(trifluoromethyl)phenyl)-fusidic acid (Compound 185),
24-(3,4-dimethoxyphenyl)-fusidic acid (Compound 186),
24-(3,5-dibromophenyl)-fusidic acid (Compound 187),
24-bromofusidic acid, cholin salt (Compound 188),
24-bromofusidic acid, L-arginine salt (Compound 189),
24-bromofusidic acid, 2-(dimethylamino)-ethanol salt (Compound 190),
24-bromofusidic acid, 4-(2-hydroxyethyl)-morpholin salt (Compound 191),
24-bromofusidic acid, L-lysine salt (Compound 192),
24-bromofusidic acid, N-(2-hydroxyethyl)-pyrrolidine salt (Compound 193),
24-bromofusidic acid, ethanolamine salt (Compound 194),
24-bromofusidic acid, potassium salt (Compound 195),
24-bromofusidic acid, tetrabutylammonium salt (Compound 196),
24-bromofusidic acid, benzyltrimethylammonium salt (Compound 197),
24-bromofusidic acid, cetyltrimethylammonium salt (Compound 198),
24-bromofusidic acid, tetramethylammonium salt (Compound 199),
24-bromofusidic acid, tetrapropylammonium salt (Compound 300),
24-bromofusidic acid, tris(hydroxymethyl)aminomethane salt (Compound 301),
24-bromofusidic acid, N-methyl-D-glucamine salt (Compound 302),

24-bromofusidic acid, silver salt (Compound 303),
24-bromofusidic acid, benzethonium salt (Compound 304),
24-bromofusidic acid, triethanolamine salt (Compound 305),
24-(*trans*-1-hexen-1-yl)-fusidic acid pivaloyloxymethylester (Compound 306),
with 24-(*trans*-1-buten-3,3-dimethyl-1-yl)-fusidic acid pivaloyloxymethyl ester (Compound 307),
24-(*trans*-1-nonen-1-yl)-fusidic acid pivaloyloxymethyl ester (Compound 308),
24-(*trans*-5-chloro-1-penten-1-yl)-fusidic acid pivaloyloxymethyl ester (Compound 309),
24-(*trans*-2-phenyl-1-vinyl)-fusidic acid pivaloyloxymethyl ester (Compound 310),
24-(2-phenyl-1-ethyl)-fusidic acid pivaloyloxymethyl ester (Compound 311),
24-(4-*n*-propylphenyl)-fusidic acid pivaloyloxymethyl ester (Compound 312),
24-(4-vinylphenyl)-fusidic acid pivaloyloxymethyl ester (Compound 313),
24-(4-*tert*-butylphenyl)-fusidic acid pivaloyloxymethyl ester (Compound 314),
24-(4-cyanophenyl)-fusidic acid pivaloyloxymethyl ester (Compound 315),
24-(3-biphenyl)-fusidic acid pivaloyloxymethyl ester (Compound 316),
24-(4-(trifluoromethyl)phenyl)-fusidic acid pivaloyloxymethyl ester (Compound 317),
24-(4-methoxyphenyl)-fusidic acid pivaloyloxymethyl ester (Compound 318),
24-(3-cyanophenyl)-fusidic acid pivaloyloxymethyl ester (Compound 319),
24-(2-methoxyphenyl)-fusidic acid pivaloyloxymethyl ester (Compound 320),
24-(3-nitrophenyl)-fusidic acid pivaloyloxymethyl ester (Compound 321),
24-(3-bromophenyl)-fusidic acid pivaloyloxymethyl ester (Compound 322),
24-(4-(methylthio)phenyl)-fusidic acid pivaloyloxymethyl ester (Compound 323),
24-(2-naphtyl)-fusidic acid pivaloyloxymethyl ester (Compound 324),
24-(3,5-*bis*-(trifluoromethyl)phenyl)-fusidic acid pivaloyloxymethyl ester (Compound 325),
24-(3,4-dimethoxyphenyl)-fusidic acid pivaloyloxymethyl ester (Compound 326), and
24-(3,5-dibromophenyl)-fusidic acid pivaloyloxymethyl ester (Compound 327).

21. A compound according to claim 1 for use in therapy.

22. A pharmaceutical composition comprising a compound according to claim 1 or 20 together with a pharmaceutically acceptable excipient or vehicle.

23. A pharmaceutical composition according to claim 22 further comprising another therapeutically active compound is selected from the group consisting of antibiotics and corticosteroids.

24. A pharmaceutical composition according to claim 23, wherein said other therapeutically active compound is selected from the group consisting of penicillins (phenoxymethyl penicillin, benzyl penicillin, dicloxacillin, ampicillin, amoxicillin, pivampicillin, flucloxacillin, piperacillin and mecellinam), cefalosporins (cefalexin, cefalotin, cefepim, cefotaxim, ceftazidim, ceftriazon and cefuroxim), monobactams (aztreonam) and carbapenems (meropenem); macrolides (azithromycin, clarithromycin, erythromycin and roxithromycin); polymyxins (colistin); tetracyclins (tetracycline, doxycyclin, oxytetracyclin and lymecyclin); aminoglycosides (streptomycin, gentamicin, tobramycin and netilmicin); fluoroquinolones (norfloxacin, ofloxacin, ciprofloxacin and moxifloxacin); clindamycin, lincomycin, teicoplanin, vancomycin, oxazolidones (linezolid), rifamycin, metronidazol, fusidic acid, hydrocortisone, betamethason-17-valerate and triamcinolone acetonid.

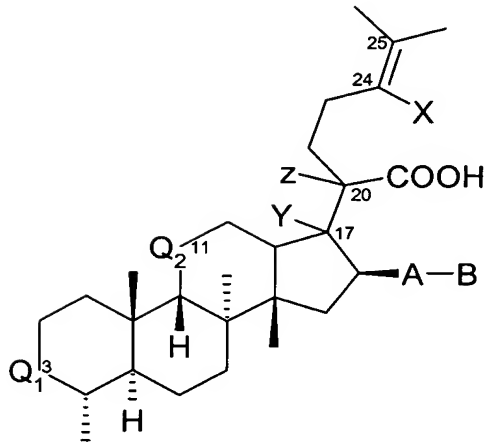
25. A method of treating, preventing or ameliorating infections in a patient, the method comprising administering to said patient an effective amount of a compound according to claim 1 or 20, and optionally further comprising concomitant or sequential administration of one or more other therapeutically active compounds.

26. A method according to claim 25, wherein said other therapeutically active compound is selected from the group consisting of antibiotics and corticosteroids.

27. A method according to claim 25, wherein said other therapeutically active compound is selected from the group consisting of of penicillins (phenoxymethyl penicillin, benzyl penicillin, dicloxacillin, ampicillin, amoxicillin, pivampicillin, flucloxacillin, piperacillin and mecellinam), cefalosporins (cefalexin, cefalotin, cefepim, cefotaxim, ceftazidim, ceftriazon and cefuroxim), monobactams (aztreonam) and carbapenems (meropenem); macrolides (azithromycin, clarithromycin, erythromycin and roxithromycin); polymyxins (colistin); tetracyclins (tetracycline, doxycyclin, oxytetracyclin and lymecyclin); aminoglycosides (streptomycin, gentamicin, tobramycin and netilmicin); fluoroquinolones (norfloxacin, ofloxacin, ciprofloxacin and moxifloxacin); clindamycin, lincomycin, teicoplanin, vancomycin, oxazolidones (linezolid), rifamycin, metronidazol, fusidic acid, hydrocortisone, betamethason-17-valerate and triamcinolone acetonid.

28. A method according to claim 25, wherein said infection is a bacterial infection.

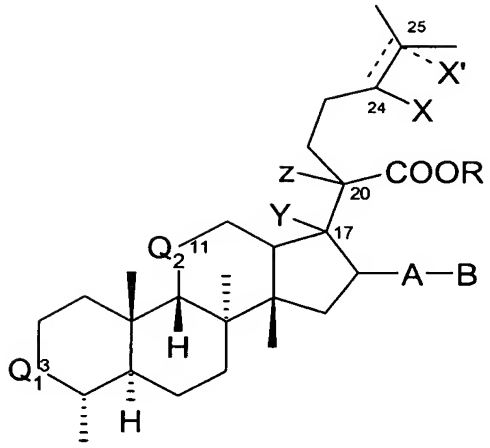
29. A method of preparing a compound of formula Ia,



[Ia]

wherein X represents bromo, Y and Z both represent hydrogen, or together with the C-17/C-20 bond form a double bond between C-17 and C-20, or together are methylene and form a cyclopropane ring in combination with C-17 and C-20; A represents a bond, O, S or S(O); B represents C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} acyl, C_{3-7} cycloalkylcarbonyl or benzoyl, all of which are optionally substituted with one or more substituents selected from the group consisting of halogen, hydroxy, C_{1-6} alkoxy, aryl, heterocyclyl and azido, or, if A represents a bond, B may also represent hydrogen; Q_1 and Q_2 independently represent -C(O)-, -(CHOH)-, -(CHSH)-, or –(CHW)-, wherein W represents halogen, cyano, azido or trifluoromethyl, the method comprising

(a) dissolving fusidic acid or a suitable fusidic acid analogue in a suitable organic solvent followed by treatment with bromine to give a 24,25-dibromo intermediate of general structure Ib,



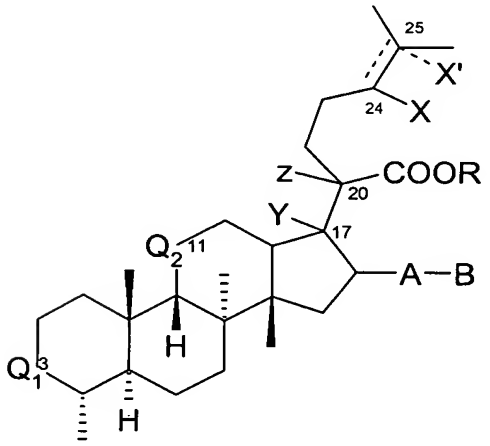
[Ib]

wherein X and X' represent bromo, R is hydrogen, the bond between C-24 and C-25 is a single bond, and Y, Z, A, B, Q_1, and Q_2 are as defined above;

(b) treating a solution of the 24,25-dibromo intermediate in a suitable solvent in the presence of a suitable base to give the dehydrobrominated compound of formula Ia, in the form of a salt; and

(c) acidifying the salt generated in step (b) to obtain the compound of formula Ia in free acid form.

30. A compound of general structure Ib,



[Ib]

wherein X and X' represent bromo, R is hydrogen, the bond between C-24 and C-25 is a single bond, Y and Z both represent hydrogen, or together with the C-17/C-20 bond form a double bond between C-17 and C-20, or together are methylene and form a cyclopropane ring in combination with C-17 and C-20, A represents a bond, O, S or

S(O); B represents C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} acyl, C_{3-7} cycloalkylcarbonyl or benzoyl, all of which are optionally substituted with one or more substituents selected from the group consisting of halogen, hydroxy, C_{1-6} alkoxy, aryl, heterocyclyl and azido, or, if A represents a bond, B may also represent hydrogen; Q_1 and Q_2 independently represent -C(O)-, -(CHOH)-, -(CHSH)-, or –(CHW)-, wherein W represents halogen, cyano, azido or trifluoromethyl.